DOI: https://doi.org/10.53350/pjmhs20231711507

ORIGINAL ARTICLE

Comparison of Effectiveness of Modified Del Nido Vs Conventional Del Nido Cardioplegia in Cardiac Surgery

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ABSTRACT

Background: Myocardial protection during cardiac surgery is crucial to minimize ischemic injury and postoperative complications. Del Nido cardioplegia (DNC), originally developed for pediatric patients, has gained widespread use in adult cardiac surgery due to its long-acting myocardial arrest properties. However, its high crystalloid content raises concerns of hemodilution and myocardial edema. Modified Del Nido cardioplegia (MDN), with a reversed blood-to-crystalloid ratio (4:1), aims to overcome these limitations while maintaining adequate myocardial protection.

Objective: This study compared the clinical effectiveness of Modified Del Nido versus Conventional Del Nido cardioplegia in adult cardiac surgery patients undergoing cardiopulmonary bypass (CPB).

Methods: A prospective, cross-sectional, non-interventional study was conducted at the Punjab Institute of Cardiology, Lahore, including 102 patients aged 18–75 years undergoing elective on-pump cardiac surgery. Group A received conventional DNC (1:4 blood-to-crystalloid), and Group B received MDN (4:1 ratio). Primary endpoints included CK-MB, CPK, hemodilution, and inotropic support. Secondary endpoints were aortic cross-clamp time, CPB duration, and postoperative ventilation time. Statistical analysis was performed using SPSS v20, with significance set at $p<0.05$.

Results: MDN cardioplegia demonstrated significantly lower CK-MB levels at 12 hours postoperatively ($p<0.05$), indicating reduced myocardial injury. Hemodilution and blood transfusion requirements were lower in the MDN group. ALT levels were slightly higher in MDN, while ionotropic support needs were lower in DNC ($p<0.05$*).

Conclusion: Modified Del Nido cardioplegia provided superior myocardial protection and reduced hemodilution compared to Conventional Del Nido. Further multicenter prospective studies are warranted to validate these findings and assess long-term clinical outcomes.

Keywords: Modified Del Nido cardioplegia, Conventional Del Nido cardioplegia, Myocardial protection, Cardiac surgery, Cardiopulmonary bypass

INTRODUCTION

Myocardial protection is the most important procedure in cardiac surgery. During cardiac surgeries, a hyperkalemic, hypothermic solution with other additives is used to attain cardiac arrest for getting the required myocardial protection.[1] Failure to adequately protect the myocardium may result in serious consequences, including myocardial ischemia, myocardial infarction, reperfusion injury, Low Cardiac Output Syndrome (LCOS), prolonged ICU-stay, extra and prolonged Ionotropic support and sometimes extra ventilation support.[2]

There is a list of cardioplegia solutions used to protect the myocardium during cardiopulmonary bypass surgery, but finding the optimal cardioplegic solution is still under debate. In 1990's Pedro Delnido and co-workersprepared a cardioprotective medicine, primarily for immature hearts with congenital defects. The solution, called conventional del Nido (CDN), is used to cease the myocardium because of hyperpolarizationfor a short time, allowing the surgeon to operate in the bloodless, motionless heart. It is a diluted solution (1:4, blood to crystalloid) compared to the conventional blood cardioplegia which is (4:1, blood to crystalloid), but also commonly used in adult cardiac surgery.[3]

The CDN, which was originally used in pediatric operations,is nowbeing used in adult cardiovascular surgery for providing diastolic cardioplegic arrest to the myocardium and also enabling the surgeons to work on a bloodless and motionless field to operate upon.[4] Del Nido cardioplegia provides a low-calcium, non-glucose, potassium-rich environment with other electrolyte compositions equal to the extracellular fluid, providing a longer duration of cardioplegic arrest.

The ingredients of del Nido cardioplegia are mixed with the oxygenated blood in a ratio of 1:4, 1-part blood, and 4 parts crystalloids solution.[5] However, a problem arose with blood conservation due to the high proportionof the crystalloid part. Also, epicardial and myocardial edema can be seen due to the higher crystalloid content compared to the blood.[6] This problem can be overcome by using modified del Nido (MDN) cardioplegia with a similar composition of electrolytes as the del Nido cardioplegia, except with the reverse in the composition of the crystalloid to blood ratio.[7] Due to its prolonged cardiac arrest time, favoring myocardial protection, and minimally interrupting the surgical procedure, it can used in adult cardiac surgery procedures and is gaining acceptance. Various studies showed the advantages of conventional del Nido cardioplegia over other solutions in adult cardiac surgery.[8] However, other studies showed the benefits of modified del Nido cardioplegia over other cardioplegias.[9]

Previous research has extensively examined the individual applications of conventional del Nido and modified del Nido cardioplegias in cardiac surgeries. However, limited comparative studies exist between these two cardioplegia solutions, especially evaluating their effectiveness in cardiac surgical patients within a single hospital center. This prospective, cross-sectional, non-interventional, observational study was aimed to address this gap by comparing the effectiveness of both CDN and MDN cardioplegia in cardiac surgery patients. Key primary endpoints for comparison were included hemodilution, CK-MB, CPK levels, inotropic support, ICU or hospital stay, time the patient spent on ventilator, the requirement for defibrillation shock, and the use of intra-aortic balloon (IAB). Secondary endpoints encompassed were aortic cross-clamp time and CPB time.

MATERIAL AND METHODS

The comparative cross-sectional, non-interventional, prospective study was held at the Department of Cardiac Surgery, Punjab Institute of Cardiology (PIC), Lahore. Patients intended to undergo cardiac surgery from Jan 2023 to June 2023 with CPB were to undergo the study over 1 year after approval of the synopsis were included in the study. Patients undergoing elective cardiac surgery with CPB were assigned into two groups. All operations were performed on CPB and cardiac arrest was achieved using cardioplegia solutions. Two groups were formed based on the data available. The patients who received the Conventional del Nido

Received on 10-07-2023
Accepted on 22-10-2023

cardioplegia (CDNC) were included in Group A while those receiving the Modified version of del Nido (MDNC) were included in Group B.

Inclusion Criteria: Patients between 18 and 75 years of age who were scheduled to undergo primary, elective cardiac surgery as advised by the cardiac surgeon were included in the study. Only those patients with a moderate to good left ventricular ejection fraction (EF ≥30%) as determined by echocardiography were considered eligible. These criteria ensured that participants had stable preoperative cardiac function and were suitable candidates for cardiopulmonary bypass procedures.

Exclusion Criteria: Patients younger than 18 years or older than 75 years were excluded from the study. Additionally, individuals undergoing emergency cardiac surgeries or those with a previous history of open-heart surgery (redo cases) were not included. Patients who were preoperatively on intra-aortic balloon pump (IABP) support, those requiring emergency interventions, and those scheduled for off-pump surgeries were also excluded. These exclusions were made to maintain homogeneity in the study population and to avoid confounding factors that could affect myocardial protection outcomes.

Pre-operative demographics data recovered from the data-bank record included name, age, gender, weight, height, medical registration number, flow rate, and preoperative EF according to Echo reports. The risk factors added included the patient's history of Diabetes Mellitus and Hypertension. The baseline levels of pre-operative CK-MB and CPK were also noted.

As the proposed study is non-interventional, hence, only the Institutional guidelines for anesthesia and surgical techniques for cardiac intervention were followed.

The Cardioplegia solutions used were prepared according to the institutional protocol. In the PIC, the Del Nido and Modified Del Nido Cardioplegia are routinely given to the patients. The del Nido Cardioplegia is prepared using the cold slush of 0.9% normal saline. The additives for the cardioplegia added include 16 mmol of 20% mannitol, 8.4% of sodium bicarbonate, 6.5 mmol of 2.0% Lignocaine, 2.0 grams of 50% Magnesium Sulfate and 26 mmol of potassium chloride. Blood in conventional del Nido cardioplegia is 300 ml, while in the modified del Nido Cardioplegia is 700 ml. All of the above-described composition is specified for the preparation of 1.0liter of Cardioplegia solution. For preparing the CDN, the blood-to-crystalloid ratio is taken as 1:4. For MDN, the blood-to-crystalloid ratio will be 4:1.

After the application of an aortic cross-clamp to the root of the aorta, the circulation of the heart from the systemic circulation was discontinued, and cardioplegia was given with the help of cardioplegia cannula. It is normally administered as per surgeon's preference or the patient's need, depending on the type of operation, without any bias from the author.

Intraoperative variables included the need for defibrillation shock, the need for a temporary pacemaker and the Intra-Aortic Balloon.

Defibrillation shock is defined as the need for an electric shock from a defibrillator to restore the heart's natural rhythm. A temporary pacemaker is a device used to provide electrical stimulation to the heart when the heart's conduction system cannot maintain its natural rhythm. Intra-Aortic Balloon is a mechanical assist device used to improve the coronary perfusion and reduce the work stress of the myocardium.

The following variables were studied to measure the efficiency of each cardioplegia for better cardiac protection.

Primary endpoints observed werethe degree of hemodilution, CPK, CK-MB, and ionotropic support.CK-MB and CPK were measured using either an immunochemical assay or ELISA.

The degree of hemodilution was measured using the common methods of determining Hemoglobin concentration in the blood's and CK-MB were measured using the immunometric or chemiluminescent methods, using the quantified commercial kits provided by the manufacturers. These are the enzymes present in myocardial bands. The acute increase in their levels indicates the myocardial damage during the cardiac surgery procedure.

Ionotropic support refers to the drugs that provide the strength to the myocardium for pushing blood to the systemic circulation. It is mostly used after the cardiopulmonary bypass to assist patients suffering from low cardiac output syndrome. The Ionotropic drugs include adrenaline, nor-adrenaline and dopamine in the center.

Secondary endpoints included were Aortic Cross-Clamp time, total Bypass time and Ventilation time postoperatively.

Bypass time is the time duration during which the patient is mechanically supported upon a heart-lung machine and circulation is provided by artificial means. Aortic Cross-Clamp time is defined as the time during which the heart is discontinued from the systemic circulation by applying the specially manufactured clamps for the aorta, and cardioplegia solution is introduced in the proximal part of the ascending aorta, between the heart and the cross-clamp.

Ventilation time is the number of hours a patient is on respiratory support using ventilator.

RESULTS

Data were analyzed statistically using SPSS version 20 (SPSS Inc., USA). Quantitative variables, such as age, were expressed as mean ± standard deviation. Qualitative variables, like gender, were included as frequency, proportion, and percentage. Continuous independent variables were analyzed using the student's t-test, or the Mann–Whitney test for non-normally distributed data. Categorical data was assessed with the Chi-square test. The significance level was predetermined at $p<0.05$.

Table 1: Composition of Cardioplegia

Ingredients	Del Nido Cardioplegia	Modified DNC
Isolyte-S NS (0.9%)	700ml	300ml
20 % Mannitol	16ml	16ml
50% Magnesium Sulphate	4ml	4ml
8.4% NaHCO3	13ml	13ml
7.5% Potassium Chloride	26ml	40ml
2% Lidocaine	6.5ml	6.5ml
Blood	300ml	700ml

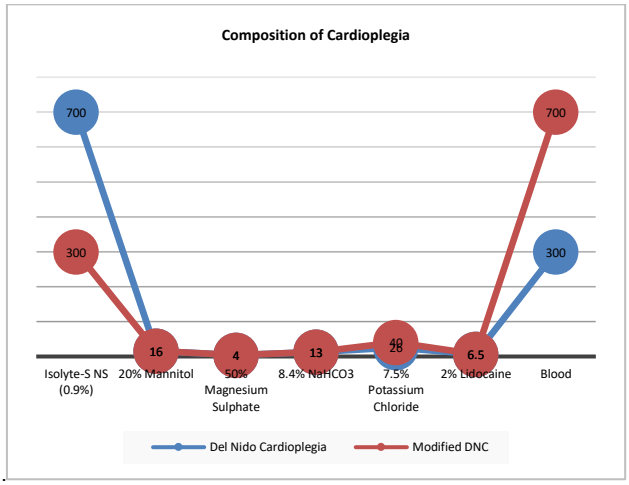

Figure 1: illustrates the procedural or graphical representation related to cardioplegia use

Table 2 shows the baseline demographic and clinical characteristics of both groups. The Blood Urea Nitrogen (BUN) for the MDN group was 25.17 ± 8.46 mg/dL, while for the DNC group it was 28.86 ± 8.16 mg/dL, with a non-significant p-value of 0.491. The serum creatinine level for MDN was 0.88 ± 0.21 mg/dL, whereas the DNC group showed 0.96 ± 0.20 mg/dL (p = 0.491).

The mean preoperative hemoglobin level was 13.89 ± were not statistically significant (p > 0.05).

Table 2: Comparison of Baseline Characteristics Between Groups

Variable	Group A (Mean ± SD / n)	Group B (Mean ± SD / n)	p-value
Age (years)	46.35 ± 15.93	44.66 ± 16.26	0.541
Gender (Male)	38	44	0.014
Weight (kg)	66.01 ± 15.21	64.99 ± 23.52	0.682
Height (cm)	160.15 ± 22.09	162.86 ± 23.50	0.549
Body Surface Area (m^2)	1.70 ± 0.28	1.67 ± 0.26	0.586
Hypertension (Number)	34	28	0.245
Ejection Fraction (%)	49.92 ± 13.77	52.83 ± 10.26	0.195
Flow Rate (L/min)	4.11 ± 0.67	4.02 ± 0.72	0.449

Table 3: Comparison of Laboratory Parameters Between MDN and DNC Groups

Parameter	MDN (n=54)	DNC (n=48)	p-value
Blood Urea (mg/dL)	25.17 ± 8.46	28.86 ± 8.16	0.717
Serum Creatinine (mg/dL)	0.88 ± 0.21	0.96 ± 0.20	0.491
Serum Bilirubin (mg/dL)	0.51 ± 0.27	0.61 ± 0.34	0.472
Hemoglobin (g/dL)	13.89 ± 2.39	14.14 ± 2.71	0.385
ALT (Alanine Transaminase) (U/L)	32.92 ± 24.06	28.00 ± 13.84	0.049

The primary end points noted included were Cardiac Enzymes Profile (Creatinine Kinase Myocardial Band, Creatinine Phosphokinases), and Hemoglobin difference. The intra-operative parameters noted included Defibrillation Shock requirements, Temporary pacemaker need and use of Intra-Aortic Balloon. The cardiac enzymes were noted at different point of times including pre-operative value, value within 12 hours after shifting from operation theatre and finally 24 hours after shifting to Intensive Care Unit The p-values of CK-MB for the pre-operative value and 24 hours after surgery were observed to be insignificant. While the 12 hours post-operatively value noted was clinically significant ($p<0.05$). Also, the values noted for CPK were at preoperative, 12 hours and 24 hours postoperative time interval, showed clinically insignificant results ($p>0.05$). These were measured in ng/L units. The difference of Haemoglobin noted between preoperative and postoperative period for MDN was having an insignificant p-value($p>0.05$). However, the total blood transfused for the MDN as a group were 66, while that of DNC were 93. The Ionotropic support for adrenaline, having a statistically significant p value($p<0.05$) at day 2 only while others were statistically insignificant. The Noradrenaline requirement at Day 0, Day1 and Day 2 was statistically significant. The CK-MB levels at 12 hours were significantly higher in the DNC group, indicating the greater myocardial injury ($p<0.05$). There is a sharp rise noted in 12 and 24-hour values of Cardiac Enzymes

DISCUSSION

The present study presents the retrospective monocentric tertiary care hospital medical records in which the two types of solutions called cardioplegias are routinely used during the on-pump cardiac surgery procedure in hospital practice. The study included two solutions named del Nido and modified del Nido cardioplegia, aimed to find the one which gives better myocardial protection. Despite the favorable and routine use of DNC solutions in many hospital settings, there are concerns regarding the use of this solution in adult cardiac patients. The advantage of Delnido is that it is delivered in a single shot with prolonged arrest time, but with the concern that it is not yet conclusive. Also, the Cleveland Clinic recommends the use of DNC for cardiac surgeries other than the coronary artery bypass grafting. Also, the use of MDN, having the ratio of 4:1 Blood to Crystalloid, has both advantages and disadvantages, yet its clinical advantages remain to be further validated. This also provides the advantage of arresting the myocardium for up to 90 minutes following the induction dose, with less hemodilution as compared to the DNC, with blood having its great buffering capacity.[10]

Thus, it is necessary to address the topic and to find the optimal solution, having results better as compared to each other. Therefore, we managed to conduct a retrospective monocentric analysis. In our study design, the degree of hemodilution in the MDN group, in terms of mean haemoglobin, difference in haemoglobin, pre-surgery, vs post-surgery, was significantly less as compared to the DNC group, having the larger use of crystalloid as a base solution. The total blood transfusion in MDN group,1.75±0.58, was less than DNC group, 1.91±0.94, but was not statistically significant. Thus, showing better results in terms of hemodilution for MDN as compared to the DNC group. Also, hemodilution during the CPB causing hematocrit less than 24% is linked to renal damage, leading to kidney injury and causing the serious outcomes of renal failure and organ damage.[11]

It is suggested that post-operative levels of CK-MB can independently predict the patient's risk of death in intermediate (12 months) or long-term (>12 months) following a major cardiovascular event.[12]

In our study, we noticed a significantly lower rise of peak CK-MB concentration for the MDN group than the DNC group. Also, some other studies reported elevated levels of CK-MB in the crystalloid cardioplegia group recipients as compared to the blood-rich cardioplegia solutions. Further, a recent study analysis comparing different studies on the blood-rich cardioplegia solution shows that patients receiving blood-rich cardioplegia solutions have a more spontaneous return of heartbeat after cross-clamp removal, compared to those receiving the crystalloid-rich cardioplegia. Also, favoring the shorter stay in the ICU.[13]

Systemic inflammatory response, in response to contact external surface, is blood, generally causing systemic generalised vasodilation. Catecholamines (adrenaline & nor-adrenaline) have been commonly used to combat this condition. Also, after weaning off CPB, low cardiac output syndrome is common, which is also combated by these catecholamines, a few hours after surgery. (Currigan et al.2014). The ionotropic support usually started after weaning off from CPB may also be associated with morbidity and mortality.[14]

In our study, the DNC group had less need for ionotropic support, and results showed that the difference is statistically significant ($p<0.05$) in comparison to the MDN group for both adrenaline and noradrenaline. The need for catecholamines as inotropes was used in our sample size; however, no requirement for dopamine was needed in our population.

CONCLUSION

Our clinical results indicate the superiority of the provision of myocardial protection by the use of MDN over DNC in cardiac surgery patients. Due to the observational, retrospective and single-center-based study design, further studies with a prospective, multicenter and, observing the long-term clinical effects, can further support or explain its efficacy and effectiveness.

Limitations: Being a single center based and, cross-sectional, retrospective observational in nature of the study design and of limited duration, further studies with a prospective multi-design may result in more detailed and conclusive clinical information concerning the efficacy of MDN cardioplegia. Further, the patient's medical record was only noted for short-term post-surgery, particularly during the hospital stay of the patient. Thus, the long-term effects need to be assessed.

Conflicts of Interest: The authors declare no conflicts of interest.

Funding: This study received no external funding.

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This article may be cited as: Shahid R, Ismael M, Umair MM: Comparison of Effectiveness of Modified Del Nido Vs Conventional Del Nido Cardioplegia in Cardiac Surgery. Pak J Med Health Sci, 2023;17(11):507-510.